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# sequence Listing

- (1) GENERAL INFORMATION:
  - (i) APPLICANT: Hewick, Rodney M. Wang, Jack H. Wozney, John M.

Celeste, Anthony J.

- (ii) TITLE OF INVENTION: Bone and Cartilage Inductive Proteins
- (iii) NUMBER OF SEQUENCES: 15
- (iv) CORRESPONDENCE ADDRESS:
  - (A) ADDRESSEE: Legal Affairs, Genetics Institute, Inc.
  - (B) STREET: 87 CambridgePark Drive
  - (C) CITY: Cambridge
  - (D) STATE: MA
  - (E) COUNTRY: USA
  - (F) ZIP: 02140
- (v) COMPUTER READABLE FORM:
  - (A) MEDIUM TYPE: Floppy disk
  - (B) COMPUTER: IBM PC compatible
  - (C) OPERATING SYSTEM: PC/DOS/MS-DOS
  - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) CURRENT APPLICATION DATA:
  - (A) APPLICATION NUMBER: US 08/319,831
  - (B) FILING DATE: 06-QCT-1994
  - (C) CLASSIFICATION
- (viii) ATTORNEY/AGENT INFORMATION:
  - (A) NAME: Kapinøs, Ellen J.
  - (B) REGISTRATION NUMBER: 32,245
  - (C) REFERENÇÉ/DOCKET NUMBER: GI 5182A-DIV
  - (ix) TELECOMMUNICATION INFORMATION:
    - (A) TELEPHONE: 617-876-1170
    - (B) TELEFAX: 617-876-5851
- (2) INFORMATION FOR SEQ ID NO:1:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A)/LENGTH: 23 amino acids
    - (B) TYPE: amino acid
    - (¢) STRANDEDNESS: single
    - (D) TOPOLOGY: unknown
  - (ii) MOLECULE TYPE: peptide
  - (i/i) HYPOTHETICAL: NO

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	(iv) ANTI-SENSE: NO
	(vi) ORIGINAL SOURCE: (F) TISSUE TYPE: Bone
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
	Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Asp 1 5 10 15
	Val Ile Ala Pro Gln Gly Tyr 20
	(2) INFORMATION FOR SEQ ID NO:2:
<i>K</i> /	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 18 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: unknown
	(ii) MOLECULE TYPE: peptide
	(iii) HYPOTHETICAL: NO
	(iv) ANTI-SENSE: NO
	(v) FRAGMENT TYPE: internal
	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Bos taurus  (F) TISSUE TYPE: Bone
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:
	Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile 1 5 10 15
	Leu Arg
	(2) INFORMATION FOR SEQ ID NO:3:
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 7 amino acids  (B) TYPE: amino acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: unknown  (ii) MOLECULE TYPE: peptide
	(ii) MYDECOLE I I FE. peptide

43 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Bos taurus (F) TISSUE TYPE: Bone (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3: Ala Cys Cys Ala Pro Thr Lys (2) JNFORMATION FOR SEQ ID NO:4: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Bos taurus (F) TISSUE TYPE: Boxe (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4: Thr Asn Glu Leu Pro Pro Pro Asn Lys Leu Pro Gly Ile Phe Asp Asp 10 Val His Gly Ser/His Gly Arg 20 (2) INFORMATION FOR SEQ ID NO:5: (i) SEQUENCE CHARACTERISTICS: (A)/LENGTH: 80 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (fii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE: (A) ORGANISM: Bos taurus (vii) IMMEDIATE SOURCE: (B) CLONE: acc30 (viii) POSITION IN GENOME: (C) UNITS: bp (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 25..57 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5 GGATCCGCGT GCTGTGCTCC GACC AAG OTG AGC GCC ACC TCC GTG CTC TAC 51 Lys Leu Ser Ala Thr Ser Wal/Leu Tyr 1 TAC GAC AGCAGCAACA ATGTAATTET AGA 80 Tyr Asp 10 (2) INFORMATION FOR SEQ ID NO:6: (i) SEQUENCE CHARA TERISTICS: (A) LENGTH: 11 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6: Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp 10 5 (2) INFORMATION FOR SEQ ID NO:7: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 199 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (if) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Bos taurus (vii) IMMEDIATE SOURCE: (A) LIBRARY: Bovine genomic (B) CLONE: Lambda 9800-10 (viii) POSITION IN GENOME: (C) UNITS: bp (ix) FEATURE: (A) NAME/KEY: exon (B) LOCATION: 30..199 (ix) FEATURE: (A) NAME/KEY: intron (B) LOCATION: 1..29 (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 30..179 (xi) SEQUENCE DESCRIPTION: SEQ ID-NO:7: TGCCCGCTGC CCCCCGC CCCCGCCAG GTG CAC CTG CTG AAG CCG CAC GCG 53 Val His Len Leu Lys Pro His Ala GTC CCC AAG GCG TGC TG/C GCG CCC ACC AAG CTG AGC GCC ACT TCC GTG 101 Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val 15 20 CTC TAC TAC GAC AGC AGC AAC AAC GTC ATC CTG CGC AAG CAC CGC AAC 149 Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asn 25 ATG GTG GTC CGC GCC TGC GGC TGC CAC TGAGGCCCCA ACTCCACCGG 196 Met Val Val Arg Ala Cys Gly Cys His 45 199 CAG (2) INFORMATION FOR SEQ ID NO:8: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 49 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Val His Leu Leu Lys Pro His Ala Val Pro Lys Ala Cys Cys Ala Pro

1 5 10 15

Thr Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn 20 25 30

Val Ile Leu Arg Lys His Arg Asn Met Val Val Arg Ala Cys Gly Cys
35 40 45

His

## (2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS
  - (A) LENGTH: 172 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double/
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DXA/(genomic)
- (iii) HYPOTHETICAL: MO
- (vi) ORIGINAL SOURCE:

(A) ORGANISM: Bos taurus

- (vii) IMMEDIATE SOURCE:
  - (A) LIBRARY: Bovine genomic
  - (B) CLONE: Lambda 9800-10
- (viii) POSITION IN GENOME:
  - (C) UNITS: bp
  - (ix) FEATURE:
    - (A) NAME/KEY: exon
    - (B) LOCATION: 51..161
- (ix) FEATURE:
  - (A) NAME/KEY: intron
  - (B) LOCATION: 1..50
- (ix) FEATURE:
  - (A) NAME/KEY: intron
  - (B) LOCATION: 162..172
- (ix) FEATURE:
  - (A) NAME/KEY: CDS
  - (B) LOCATION: 51..161

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9: GGGGTGGGAG GGCACGTGGA TGGGACTCAC CTTCTCCCAC TACCCCCCAG GAC TGG 56 Asp Trp 1 GTC ATC GCC CCC CAA GGC TAC TCA GCC TAT TAC TGT GAA GGG GAG TGC 104 Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys 10 TCC TTC CCG CTG GAC TCC TGC ATG AAC GCC ACC AAC CAC GCC ATC CTG 152 Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu 172 CAG TCC CTG GTCAGTACCT C Gln Ser Leu 35 (2) INFORMATION FOR SEQ ID NO:10, (i) SEQUENCE CHARACTERISTICS (A) LENGTH: 37 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10: Asp Trp Val Ile Ala Pro Gly Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly 10 Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu Gln Ser Leu 35 (2) INFORMATION FOR SEQ ID NO:11: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 119 base pairs (B)/TYPE: nucleic acid (Q) STRANDEDNESS: double (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO

(vi) ORIGINAL SOURCE:	
(A) ORGANISM: Bos taurus	
(vii) IMMEDIATE SOURCE:	
(A) LIBRARY: Bovine genous	
(B) CLONE: Lambda 9800-10	
(viii) POSITION IN GENOME:	
· '	
(C) UNITS: bp	
(ix) FEATURE:	
(A) NAME/KEY: exon	
(B) LOCATION: 2099	
(ix) FEATURE:	
(A) NAME/KEY: intron	
(B) LOCATION: 119	
(B) LOCATION: 1::19	
(ix) FEATURE:	
(A) NAME/KEY: intron	
(B) LOCATION: 100119	
(2) 20 31110111 /	
(ix) FEATURE:	
(A) NAME/KEY: CDS	
(B) LOCATION: 2299 /	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:	
CCCTTGCGTG TCCCCGCAGA C GAC GTC CAC GGC TCC CAC G	GC CGG CAG GTG 51
Asp Yal His Gly Ser His Gly Arg Gln Val	
$\frac{1}{1}$ $\frac{1}{5}$ $\frac{10}{10}$	^
TGC CGT CGG CAC GAG CTG TAC GTG AGC TTC CAG GAC CTG	G GGC TGG CTG 99
Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu	
15 / 20 25	
GTGAGTTCCG ACTCTCCTTT 1	19
GIGNOTICES NETEROLITY	. •
(2) INFORMATION FOR SEQ ID NO:12:	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 26 amino acids	
(B) TYPE: amino acid	
(D) TOPOLOGY: linear	
(b) 101 02001. Illion	
/(ii) MOLECULE TYPE: protein	

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12: Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His Glu Leu 15 1 5 Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu (2) INFORMATION FOR SEQ ID NO:13: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1003 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular (ii) MOLECULE TYPE: cDNA to mRNA (iii) HYPOTHETICAL: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Hopmo sapiens (F) TISSUE TYPE: Human Meart (vii) IMMEDIATE SOURCE: (A) LIBRARY: Human heart cDNA library stratagene catalog #936208 (B) CLONE: hH38 (viii) POSITION IN GENOME: (C) UNITS: bp (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 8..850 (ix) FEATURE: (A) NAME/KEY: mat peptide (B) LOCATION: 427..843 (ix) FEATURE: (A) NAME/KEY: mRNA (B) LOCATION: 1..997 (x/) SEQUENCE DESCRIPTION: SEQ ID NO:13: GAATTCC GAG CCC CAT TGG AAG GAG TTC CGC TTT GAC CTG ACC CAG ATC 49 Glu Pro His Trp Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile -135 -130 -139

Pro Ala Gly Glu Ala Val Thr Ala Ala G		97
-125 -120 -115	-110	
CCC AGC ATC CAC CTG CTC AAC A Pro Ser Ile His Leu Leu Asn Arg Thr Le -105 -100	AGG ACC CTC CAC GTC AGC ATG TTC CAG eu His Val Ser Met Phe Gla -95	145
GTG GTC CAG GAG CAG TCC AAC Val Val Gln Glu Gln Ser Asn Arg Glu S -90 -85	AGG GAG TCT GAC TTG TTC TTT TTG GAT  Ser Asp Leu Phe Phe Leu Asp  -80	193
Leu Gln Thr Leu Arg Ala Gly Asp Glu	GAC GAG GCC TGG CTG GTG CTG GAT GTC Gly Trp Leu Val Leu Asp Val -65	241
ACA GCA GCC AGT GAC TGC TGG Thr Ala Ala Ser Asp Cys Trp Leu Leu I -60 -55 -50		289
CTC CGC CTC TAT GTG GAG ACT C Leu Arg Leu Tyr Val Glu Thr Glu Asp -45 -40 -35	GAG GAT GGG CAC AGC GTG GAT CCT GGC Gly His Ser Val Asp Pro Gly -30	337
CTG GCC GGC CTG CTG GGT CAA Leu Ala Gly Leu Leu Gly Gln Arg Ala -25 -20	CGG-CCC CCA CGC TCC CAA CAG CCT TTC Pro Arg Ser Gln Gln Pro Phe -15	385
GTG GTC ACT TTC TTC AGG GCC AVal Val Thr Phe Phe Arg Ala Ser Pro S	AGT CCG AGT CCC ATC CGC ACC CCT CGG er Pro Ile Arg Thr Pro Arg 1	433
GCA GTG AGG CCA CTG AGG AGG Ala Val Arg Pro Leu Arg Arg Arg Gln 5 10 15	AGG CAG CCG AAG AAA AGC AAC GAG CTG Pro Lys Lys Ser Asn Glu Leu	481
CCG CAG GCC AAC CGA CTC CCA Pro Gln Ala Asn Arg Leu Pro Gly Ile P 20 25 30	GGG ATC TTT GAT GAC GTC CAC GGC TCC he Asp Asp Val His Gly Ser 35	529
CAC GGC CGG CAG GTC TGC CGT His Gly Arg Gln Val Cys Arg Arg His 6 40 45	CGG CAC GAG CTC TAC GTC AGC TTC CAG Glu Leu Tyr Val Ser Phe Gln 50	577
GAC CTT GGC TGG CTG GAC TGG Asp Leu Gly Trp Leu Asp Trp Val Ile A	GTC ATC GCC CCC CAA GGC TAC TCA GCC Ala Pro Gln Gly Tyr Ser Ala 65	625
TAT/TAC TGT GAG GGG GAG TGC Tyr/Tyr Cys Glu Gly Glu Cys Ser Phe I 70 75	TCC TTC CCG CTG GAC TCC TGC ATG AAC Pro Leu Asp Ser Cys Met Asn 80	673

GCC ACC AAC CAC GCC ATC CTG CAG TCC CTG GTG CAC CTG ATG AAG CCA  721  Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro  85  90  95
AAC GCA GTC CCC AAG GCG TGC TGT GCA CCC ACC AAG CTG AGC GCC ACC  Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr  100 105 110 115
TCT GTG CTC TAC TAT GAC AGC AGC AAC AAC GTC ATC CTG CGC AAG CAC  817 Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His  120  125  130
CGC AAC ATG GTG GTC AAG GCC TGC GGC TGC CAC TGAGTCAGCC CGCCCAGCCC  870  Arg Asn Met Val Val Lys Ala Cys Gly Cys His  135  140
TACTGCAGCC ACCCTTCTCA TCTGGATCGC GCCCTGCAGA GGCAGAAAAC CCTTAAATGC 93
TGTCACAGCT CAAGCAGGAG TGTCAGGGGC CCTCACTCTC GGTGCCTACT TCCTGTCAGG 99
CTTCTGGGAA TTC 1003
(2) INFORMATION FOR SEQ ID NO: 14:
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 281 amino acids  (B) TYPE: amino acid  (D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:
Glu Pro His Trp Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile Pro Ala -139 -135 -130 -125
Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Val Pro Ser -120 -115 -110
Ile His Leu Len Asn Arg Thr Leu His Val Ser Met Phe Gln Val Val -105 -100 -95
Gln Glu Gln Ser Asn Arg Glu Ser Asp Leu Phe Phe Leu Asp Leu Gln -90 -85 -80
Thr Leu Arg Ala Gly Asp Glu Gly Trp Leu Val Leu Asp Val Thr Ala -75 -70 -65 -60
Ala Ser Asp Cys Trp Leu Leu Lys Arg His Lys Asp Leu Gly Leu Arg -55 -50 -45

Leu Tyr Val Glu Thr Glu Asp Gly His Ser Val Asp Pro Gly Leu Ala
-40
-35
-30

Gly Leu Leu Gly Gln Arg Ala Pro Arg Ser Gln Gln Pro Phe Val Val -25 -20 -15

Thr Phe Phe Arg Ala Ser Pro Ser Pro Ile Arg Thr Pro Arg Ala Val
-10 -5 1 5

Arg Pro Leu Arg Arg Gln Pro Lys Lys Ser Asn Glu Leu Pro Gln
10 15 20

Ala Asn Arg Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser His Gly 25 30 35

Arg Gln Val Cys Arg Arg His Glu Leu Tyr Var Ser Phe Gln Asp Leu
40 45 50

Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr 55 60 65

Cys Glu Gly Glu Cys Ser Phe Pro Lev Asp Ser Cys Met Asn Ala Thr 70 75 80 85

Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro Asn Ala 90 95 100

Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val 105 1/10 115

Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asn 120 125 130

Met Val Val Lys Ala/Cys Gly Cys His

#### (2) INFORMATION FOR SEQ ID NO:15:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 112 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (iii)/HYPOTHETICAL: NO
- (jv) ANTI-SENSE: NO

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## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His Gly Leu

1 5 10 15 .

Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Leu Leu Val De Ala Pro 20 25 30

Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Leu 35 40 45

Asp Ser Cys Met Asn Ala Thr Asn His Ala He Leu Gln Ser Leu Val 50 55 60

His Leu Leu Lys Pro His Ala Val Pro Lys Ala Cys Cys Ala Pro Thr 65 70 75 80

Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val 85 90 95

Ile Leu Arg Lys His Arg Ash Met Val Val Arg Ala Cys Gly Cys His
100 110